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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,643	11/18/2003	Peter A. Crooks	069962-0102	2532

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

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12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,643	CROOKS ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-10,12-18,21-25,28-31 and 71* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 5-9, 12-18, 21-25, 28-31, 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 10/9/2007. Claim(s) 3-4, 11, 19-20, 26-27, 32-70, 72 have been cancelled. Claim(s) 1-2, 5-10, 12-18, 21-25, 28-31, 71 are pending. Claim(s) 1-2 have been amended. Claim(s) 10 has been withdrawn. Claim(s) 1-2, 5-9, 12-18, 21-25, 28-31, 71 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of Applicant's claim amendments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Ebert et al. (European Journal of Pharmacology, 333, 1997, 99-104).

Ketamine is taught to be a well-known NMDA receptor antagonist and has been used as an analgesic for over 30 years. In sub-anaesthetic doses the analgesic effects of ketamine are thought to be mediated by the blockade of the NMDA receptors. Norketamine is a metabolite of ketamine with similar pharmacological profiles as a NMDA receptor antagonist following an oral or i.m. dose (pg. 99-100). Therefore,

norketamine has some analgesic properties. It was determined that (S)-norketamine is approximately 8 times more potent than (R)-norketamine (pg. 102). Following oral administration of (RS)-ketamine, (S)-norketamine will be present in human plasma at sufficiently high concentrations to account for some of the observed analgesic activity. Clinical studies involving oral administration of (S)-norketamine and its reduced side effects are now being investigated in humans (pg. 103).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 5-9, 12-18, 21-25, 28-31, 71 are rejected under 35 U.S.C. 103(a) as being obvious over Ebert et al. (European Journal of Pharmacology, 333, 1997, 99-104)

as applied to claims 1-2 in view of Harbut et al. (US Patent Application 2005/0148673 A1).

The instant claims are directed to a method of treating neuropathic pain by administering (S)-norketamine over a 24-hour period and in conjunction with a narcotic analgesic effective to treat pain.

Ebert et al. teach as discussed above, however fail to disclose the specific dosage and a narcotic analgesic.

Harbut et al. teach treating neuropathic pain by administering a composition comprising NMDA receptor antagonist, such as ketamine (abstract), which can be co-administered with Valium (paragraph 0033). Ketamine can be administered intravenously and subcutaneously (paragraph 0038) and for a sustained period of time, such as two or more consecutive days (paragraph 0057). Ketamine is also disclosed to be metabolically degraded into norketamine, which is about 25% as effective as ketamine (paragraph 0081). Other pain treating drugs, such as morphine and oxycontin, were typically reduced by about 25% on the second day of treatment, while ketamine treatment continued (paragraph 0086). Typical dosage of ketamine is disclosed to be 10 mg/hour (paragraph 0100) or 240 mg per day, which meet the limitation between 0.05 to 8 mg/kg body weight or 3.5 to 1400 mg for an average adult of 70 kg.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have substituted (S)-norketamine

as disclosed by Ebert for ketamine in the composition disclosed by Harbut for treating neuropathic pain.

A person of ordinary skill in the art would have been motivated to make this substitution because: (1) both (S)-norketamine and ketamine are functionally equivalent as NMDA receptor antagonists; (2) both (S)-norketamine and ketamine are known in the prior art to have analgesic properties; (3) ketamine breaks down metabolically to (S)-norketamine; and (4) (S)-norketamine is disclosed to have fewer side effects than ketamine. Therefore, the skilled artisan would have had a reasonable expectation of success in treating neuropathic pain. Furthermore, it is obvious to one of ordinary skill in the art to have self-administered on an outpatient basis (S)-norketamine to effectively treat pain because of the convenience and ease of not having to go to the hospital as frequently and for prolonged periods of time.

Examiner notes that the dosage amounts disclosed in the rejection is inherently below a level to induce dysphoria since a composition and its properties are inseparable. It is also obvious that a physician or medical provider would prescribe such dosages so as to limit or reduce as much side effects as possible.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The

burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Response to Arguments

Applicant argues that Ebert does not disclose administration to a subject but rather in vitro assays of a rat cortical wedge preparation and a neonatal rat spinal cord preparation. Applicant continues to argue that the clinical studies are a hearsay statement and that the clinical studies never took place. Moreover, there are many steps that take place in the process of prosecuting a clinical study before administration of a drug takes place, which have not been mentioned by Ebert.

This is not persuasive because Ebert also clearly teach clinical administration in humans as evidenced by (S)-norketamine present in human plasma at sufficiently high concentrations to account for analgesic activity after oral administration (pg. 103, last paragraph). Examiner reminds Applicant that the many steps before clinical administration are not limitations that can be found in the claims, therefore are given no patentable weight.

Applicant argues that under 35 USC 102(b), a public use outside of the US is not considered prior art. Applicant goes on to claim that all of the authors of Ebert are associated with institutions in Denmark; therefore any clinical studies were performed outside of the US.

This is not persuasive because Applicant is clearly trying to spin this foreign prior art reference into a public use rejection. Applicant is reminded that the Ebert reference

is not claiming public use but rather it is a foreign reference that teaches the claimed invention.

The Kleven Declaration under 37 CFR 1.132 filed 10/9/2007 is insufficient to overcome the rejection of claims 1-2, 5-9, 12-18, 21-25, 28-31, 71 based upon Ebert et al. (European Journal of Pharmacology, 333, 1997, 99-104) and Harbut et al. (US Patent Application 2005/0148673 A1) as set forth in the last Office action because Dr. Kleven is simply stating his opinion that he thinks that (S)-norketamine was never tested in clinical trials because of the lack of any relevant publications since the Ebert reference. Again, Dr. Kleven is merely stating his opinion, which he is not 100% certain of. This does not take away or diminish the fact that Ebert clearly states that clinical trials involving the oral administration of (S)-norketamine in humans had taken place.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Applicant argues that the claimed subject matter solved a problem that was long standing in the art. However, there is no showing that others of ordinary skill in the art were working on the problem and if so, for how long. In addition, there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. See MPEP § 716.04.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC